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NEWS 8 AUG 18 FROSTI and KOSMET enhanced with Simultaneous Left and Right  
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NEWS 9 AUG 18 Simultaneous left and right truncation added to ANABSTR  
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=> file registry

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SINCE FILE

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0.21

0.21

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STRUCTURE FILE UPDATES: 28 NOV 2003 HIGHEST RN 622010-69-9  
DICTIONARY FILE UPDATES: 28 NOV 2003 HIGHEST RN 622010-69-9

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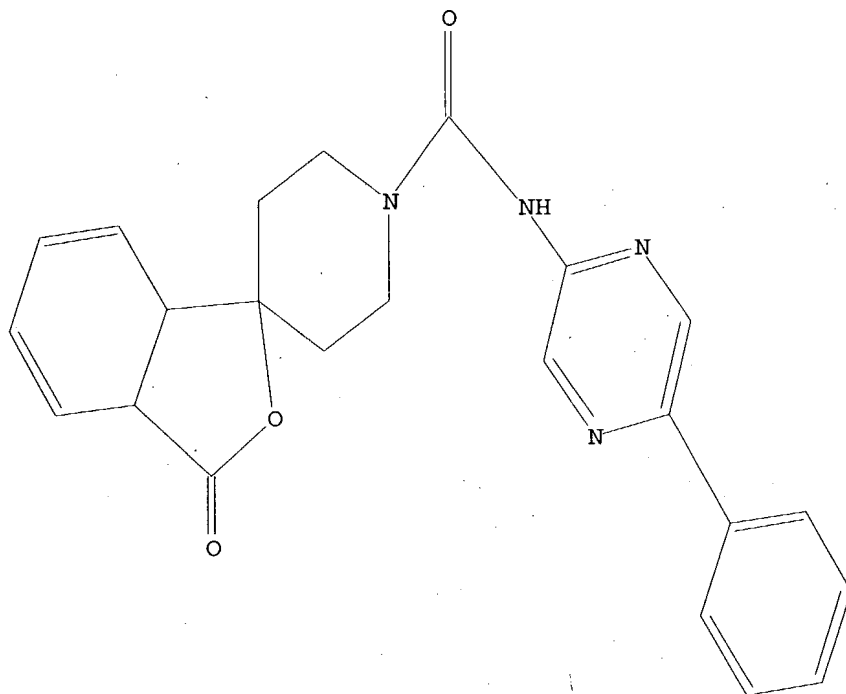
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in the CAS Registry File, for complete details:  
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=>  
Uploading 10054413.str

L1 STRUCTURE UPLOADED

=> d l1  
L1 HAS NO ANSWERS  
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss sam  
SAMPLE SEARCH INITIATED 14:10:37 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED

1 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 1 TO 80  
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 14:10:43 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 21 TO ITERATE

100.0% PROCESSED 21 ITERATIONS 8 ANSWERS  
SEARCH TIME: 00.00.01

L3 8 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	148.15	148.36

FILE 'CAPLUS' ENTERED AT 14:10:48 ON 29 NOV 2003  
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FILE COVERS 1907 - 29 Nov 2003 VOL 139 ISS 23  
FILE LAST UPDATED: 28 Nov 2003 (20031128/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3

L4 3 L3

=> s l4/prep

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=> d l4 hitstr, iall 1-3

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN

IT ~~328233-00-7P~~

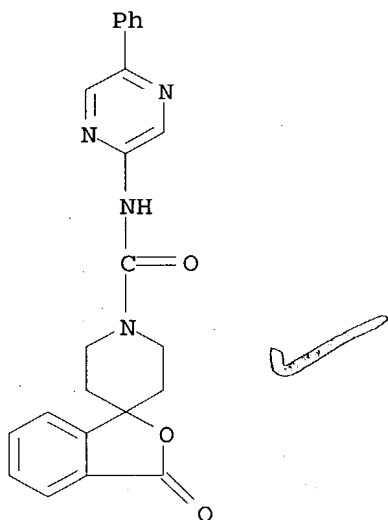
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(prepn. of spiroisindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as

neuropeptide Y antagonists)

RN 328233-00-7 CAPLUS

CN Spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide,  
3-oxo-N-(5-phenylpyrazinyl)- (9CI) (CA INDEX NAME)



IT 328232-34-4P 328232-36-6P 328232-57-1P

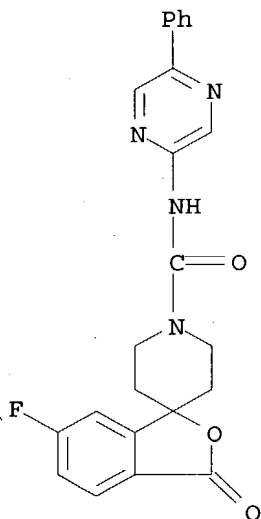
328232-58-2P 328232-61-7P 328232-62-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)

(prepn. of spiroisindolinepiperidinecarboxamides,  
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spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as  
neuropeptide Y antagonists)

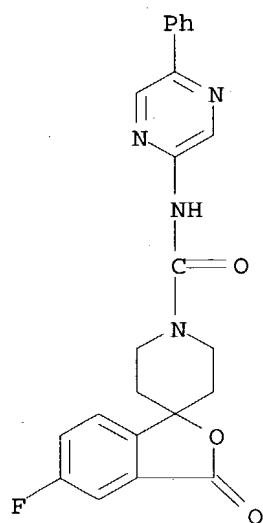
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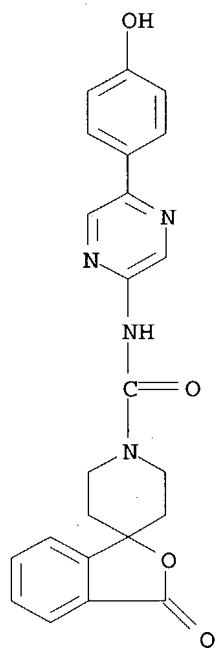


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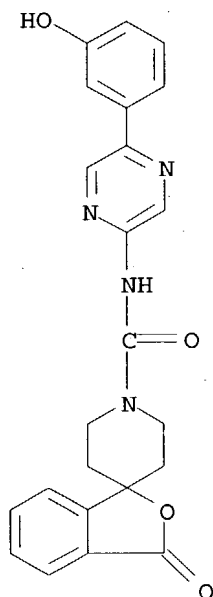
CN Spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide,  
5-fluoro-3-oxo-N-(5-phenylpyrazinyl)- (9CI) (CA INDEX NAME)



RN 328232-57-1 CAPLUS  
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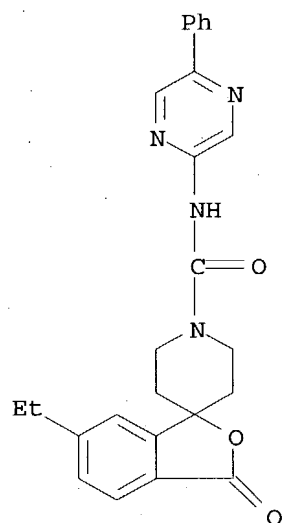


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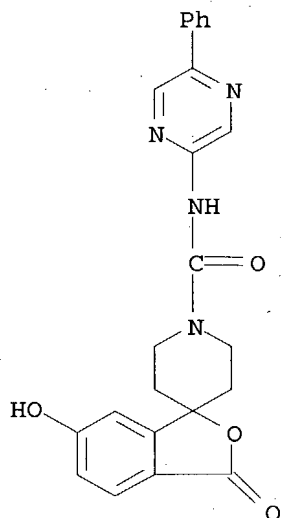
RN 328232-61-7 CAPLUS

CN Spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide,  
6-ethyl-3-oxo-N-(5-phenylpyrazinyl)- (9CI) (CA INDEX NAME)



RN 328232-62-8 CAPLUS

CN Spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide,  
6-hydroxy-3-oxo-N-(5-phenylpyrazinyl)- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 2002:947029 CAPLUS  
 DOCUMENT NUMBER: 138:24705  
 TITLE: Preparation of spiroisindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compounds as neuropeptide Y antagonists;  
 INVENTOR(S): Fukami, Takehiro; Kanatani, Akio; Ishihara, Akane; Ishii, Yasuyuki; Takahashi, Toshiyuki; Haga, Yuji; Sakamoto, Toshihiro; Itoh, Takahiro  
 PATENT ASSIGNEE(S): Japan  
 SOURCE: U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Pat. Appl. 2002 52,371.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 INT. PATENT CLASSIF.:  
     MAIN: C07D487-20  
     SECONDARY: C07D471-20  
 US PATENT CLASSIF.: 544230000; 546017000; 546018000  
 CLASSIFICATION: 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))  
     Section cross-reference(s): 1, 63  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002188124	A1	20021212	US 2002-92549	20020308
JP 2003104884	A2	20030409	JP 2002-271261	20000817
US 6026375	B1	20011204	US 2000-640784	20000818
US 6035345	B1	20020101	US 2001-928431	20010814
US 2002052371	A1	20020502	US 2001-983598	20011025
US 6388077	B2	20020514		
US 6462053	B1	20021008	US 2002-101221	20020320
US 2002165391	A1	20021107		
US 2003055251	A1	20030320	US 2002-226225	20020823
US 6649624	B2	20031118		
WO 2003076443	A1	20030918	WO 2003-JP2611	20030305

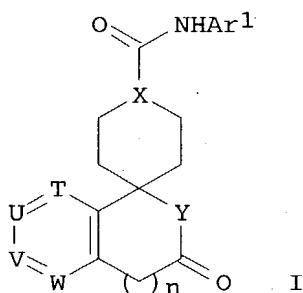
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,  
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GW, ML, MR, NE, SN, TD, TG

US 2003220499 A1 20031127  
PRIORITY APPLN. INFO.:

US 2003-453737 20030604  
JP 1999-233573 A 19990820  
JP 2000-137692 A 20000510  
US 2000-640784 A3 20000818  
US 2001-983598 A2 20011025  
JP 2000-247145 A3 20000817  
US 2002-92549 A 20020308  
US 2002-101221 A3 20020320  
US 2002-226225 A3 20020823

OTHER SOURCE(S): MARPAT 138:24705  
GRAPHIC IMAGE:



# ABSTRACT:

Title compds. [I; Ar1 = (substituted) aryl, heteroaryl, QAr2; Ar2 = (substituted) aryl, heteroaryl; Q = bond, CO; T, U, V, W = N, (substituted) CH; X = CH, CH(OH); Y = (substituted) imino, O], were prepd. Thus, N-tert-butoxycarbonyl-4-piperidone was refluxed 3 h with PhCH2NH2 in PhMe to give a residue which was stirred with o-iodobenzoyl chloride and Et3N in PhMe at 80.degree. for 2 h to give N-benzyl-N-(1-tert-butoxycarbonyl-1,2,3,6-tetrahydropyridin-4-yl)-2-iodobenzamide. The latter was heated with Pd(OAc)2, Ph3P, K2CO3, and Et4NCl in MeCN at 80.degree. for 6 h to give 2-benzyl-1'-tert-butoxycarbonyl-1',6'-dihydrospiro[1H-isoindole-1,4'(5'H)-pyridine]-3(2H)-one. This was converted to N-(4-benzoylphenyl)-3-oxospiro[isoindoline-1,4'-piperidine]-1'-carboxamide (II), which inhibited [125I]neuropeptide Y binding to NPY Y5 receptors with IC50 = 1.2 nM. II drug formulations are given.

SUPPL. TERM: spiroisoindolinepiperidinecarboxamide prepn npy antagonist;  
spirocyclohexaneisobenzofurancarboxamide  
spiroazaisobenzofurancyclohexancarboxamide prepn  
neuropeptide Y receptor antagonist; antidiabetic  
spirocyclohexaneisobenzofurancarboxamide  
spiroazaisobenzofurancyclohexancarboxamide prepn;  
antiobesity agent spirocyclohexaneisobenzofurancarboxamide  
spiroazaisobenzofurancyclohexancarboxamide prepn; bulimia  
treatment spirocyclohexaneisobenzofurancarboxamide  
spiroazaisobenzofurancyclohexancarboxamide prepn  
INDEX TERM: Appetite

(bulimia, treatment; prepn. of  
spiroisoindolinepiperidinecarboxamides,  
spirocyclohexaneisobenzofurancarboxamides,  
spiroazaisobenzofurancyclohexancarboxamides, and related  
compds. as neuropeptide Y antagonists)

INDEX TERM: Antidiabetic agents



# Antiobesity agents

## Human

(prepn. of spiroisindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as neuropeptide Y antagonists)

INDEX TERM:

Diabetes mellitus

## Obesity

(treatment; prepn. of spiroisindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as neuropeptide Y antagonists)

INDEX TERM:

82785-45-3, Neuropeptide Y

ROLE: BSU (Biological study, unclassified); BIOL (Biological study)

(antagonists; prepn. of spiroisindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as neuropeptide Y antagonists)

INDEX TERM:

328232-26-4P 328232-65-1P **328233-00-7P**

ROLE: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of spiroisindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as neuropeptide Y antagonists)

INDEX TERM:

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ROLE: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of spiroisindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as neuropeptide Y antagonists)

INDEX TERM:

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478014-43-6P	478014-44-7P	478014-45-8P	478014-55-0P

ROLE: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of spiroisindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as neuropeptide Y antagonists)

INDEX TERM:

55-22-1, Isonicotinic acid, reactions 59-67-6, Nicotinic acid, reactions 88-65-3, 2-Bromobenzoic acid 100-07-2, 4-Methoxybenzoyl chloride 102-52-3, Malonaldehyde bisdimethylacetal 107-13-1, Acrylonitrile, reactions 107-91-5, 2-Cyanoacetamide 124-68-5, 2-Amino-2-methyl-1-propanol 394-41-2, 3-Fluoro-4-nitrophenol 609-67-6, o-Iodobenzoyl chloride 619-64-7, 4-Ethylbenzoic acid 1137-41-3, 4-Aminobenzophenone 3612-20-2, 1-Benzyl-4-piperidone 4746-97-8, 1,4-Cyclohexanedione monoethylene ketal 6144-78-1, N-Methyl-2-pyridinecarboxamide 7752-82-1, 2-Amino-5-bromopyrimidine 10365-98-7, 3-Methoxyphenylboronic acid 13535-13-2, 2-Amino-5-phenylpyrazine 59489-71-3, 2-Amino-5-bromopyrazine 71597-85-8, 4-Hydroxyphenylboronic acid 79099-07-3, N-tert-Butoxycarbonyl-4-piperidone 87199-15-3, 3-Hydroxymethylphenylboronic acid 172733-79-8, 173944-49-5, 173944-52-0, 190060-72-1, 328232-95-7, 328233-38-1, 328233-39-2, 328233-40-5, 328233-41-6, 328233-44-9, 328233-45-0, 478014-40-3

ROLE: RCT (Reactant); RACT (Reactant or reagent)

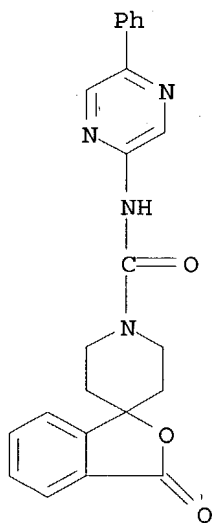
(prepn. of spiroisindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as neuropeptide Y antagonists)

INDEX TERM:

20577-26-8P, 2-Bromo-3-cyanopyridine 20577-27-9P, 3-Cyano-2-hydroxypyridine 53416-46-9P 79568-32-4P

204770-67-2P, 2-Amino-5-(4-hydroxyphenyl)pyrazine  
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 478014-39-0P 478014-41-4P  
 ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)  
 (prepn. of spiroisobenzofuranepiperidinecarboxamides,  
 spirocyclohexaneisobenzofurancarboxamides,  
 spiroazaisobenzofurancyclohexanecarboxamides, and related  
 compds. as neuropeptide Y antagonists)

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN  
 IT 471257-55-3P, 3-Oxo-N-(5-phenylpyrazinyl)spiro(isobenzofuran-  
 1(3H),4'-piperidine)-1'-carboxamide  
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP  
 (Preparation)  
 (environmentally sound process for making pyrazinyl  
 spiroisobenzofuranones by coupling aminopyrazines with spirolactones)  
 RN 471257-55-3 CAPLUS  
 CN Spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide,  
 3-oxo-N-(5-phenylpyrazinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



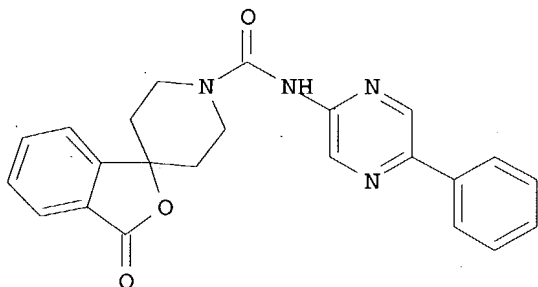
● HCl

*Applicant*

ACCESSION NUMBER: 2002:794288 CAPLUS  
 DOCUMENT NUMBER: 137:310936  
 TITLE: ~~Process for making pyrazinyl spiroisobenzofuranones~~  
 INVENTOR(S): Song, Zhiqiao Jake; Zhao, Matthew Mangzhu  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 7 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 INT. PATENT CLASSIF.:  
 MAIN: A61K007-46

US PATENT CLASSIF.: 512010000  
CLASSIFICATION: 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002151456	A1	20021017	US 2002-54413	20020122
PRIORITY APPLN. INFO.:			US 2001-263463P P	20010123
OTHER SOURCE(S):		CASREACT 137:310936		
GRAPHIC IMAGE:				



I

ABSTRACT:

This invention relates to a process for making spiroisobenzofuranones, in particular 3-oxo-N-(5-phenylpyrazinyl)spiro(isobenzofuran-1(3H),4'-piperidine)-1'-carboxamide (I), by coupling of an aminopyrazine fragment with a spirolactone piece. For the aminopyrazine fragment, the process in this invention involves a selective monobromination, a catalyzed Suzuki coupling, and carbamate formation steps. The synthesis of the spirolactone piece involves lithiation/addn. to 1-benzyl-4-piperidone, acid catalyzed cyclization, and deprotection by hydrogenolysis. Prior to the present invention, the monobromination of 2-aminopyrazine would produce a low yield of the desired product due to side reactions. However, the use of a flow-cell type reactor in the present invention significantly improves the yield. During the Suzuki coupling, the addn. of a stable cryst. solid catalyst with reliable quality improves the coupling. In addn., the present invention provides an environmentally sound process that eliminates the need to use pyridine as the solvent during the carbamate formation and chloroform in the final coupling. As a result, the present invention provides an environmentally sound procedure for making functionalized pyrazine compd. in good yields. For example, N-(5-phenyl-2-pyrazinyl)carbamate was prepd. in three steps: (1) bromination of 2-aminopyrazine using 1,3-dibromo-5,5-dimethylhydantoin in a flow-cell reactor, (2) coupling of 2-amino-5-bromopyrazine with PhB(OH)<sub>2</sub> in the presence of PdCl<sub>2</sub>.bul.dppf and K<sub>2</sub>CO<sub>3</sub>, and (3) treatment of 2-amino-5-phenylpyrazine with PhOCOCl and pyridine in MeCN and THF. Lithiation of 2-bromobenzoic acid using BuLi, followed by addn. of 1-benzyl-4-piperidone and conc. HCl in THF gave 1'-benzylspiro[isobenzofuran-1(3H),4'-piperidine]-3-one.bul.HCl. Debenzylation using 10% Pd/C and coupling with N-(5-phenyl-2-pyrazinyl)carbamate in the presence of i-Pr<sub>2</sub>NET in DMF afforded I.

SUPPL. TERM: pyrazinyl spiro isobenzofuranone piperidine prepn  
aminopyrazine spirolactam coupling; spiro isobenzofuranone  
piperidine pyrazinyl prepn green chem  
INDEX TERM: Cyclocondensation reaction  
Cyclocondensation reaction catalysts  
Green chemistry  
Suzuki coupling reaction  
Suzuki coupling reaction catalysts  
(environmentally sound process for making pyrazinyl  
spiroisobenzofuranone compds. by coupling aminopyrazines

with spirolactones)

INDEX TERM: Reactors  
(flow; environmentally sound process for making pyrazinyl spiroisobenzofuranone compds. by coupling aminopyrazines with spirolactones)

INDEX TERM: Spiro compounds  
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(lactams; environmentally sound process for making pyrazinyl spiroisobenzofuranone compds. by coupling aminopyrazines with spirolactones)

INDEX TERM: Lactams  
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(spiro; environmentally sound process for making pyrazinyl spiroisobenzofuranone compds. by coupling aminopyrazines with spirolactones)

INDEX TERM: 471257-55-3P, 3-Oxo-N-(5-phenylpyrazinyl)spiro(isobenzofuran-1(3H),4'-piperidine)-1'-carboxamide  
ROLE: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)  
(environmentally sound process for making pyrazinyl spiroisobenzofuranones by coupling aminopyrazines with spirolactones)

INDEX TERM: 98-80-6, Phenylboronic acid 1885-14-9, Phenyl chloroformate 3612-20-2, 1-Benzyl-4-piperidone 5049-61-6, 2-Aminopyrazine 25638-04-4, Bromobenzoic acid  
ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(environmentally sound process for making pyrazinyl spiroisobenzofuranones by coupling aminopyrazines with spirolactones)

INDEX TERM: 13535-13-2P, 2-Amino-5-phenylpyrazine 54596-01-9P, 1'-Benzylspiro(isobenzofuran-1(3H),4'-piperidin)-3-one Hydrochloride 59489-71-3P, 2-Amino-5-bromopyrazine 172733-79-8P, Spiro(isobenzofuran-1(3H),4'-piperidin)-3-one Hydrochloride 268538-11-0P, Phenyl N-(5-phenyl-2-pyrazinyl)carbamate  
ROLE: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(intermediate; environmentally sound process for making pyrazinyl spiroisobenzofuranones by coupling aminopyrazines with spirolactones)

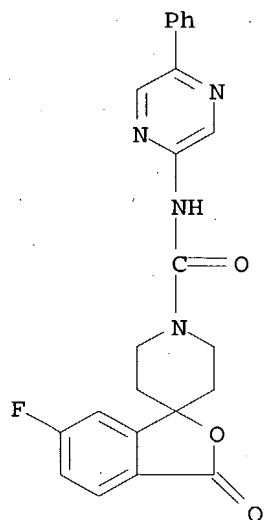
L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN

IT 328232-34-4P 328232-36-6P 328232-57-1P  
328232-58-2P 328232-61-7P 328232-62-8P  
328233-00-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of spiroisindolinepiperidines, spiroisoquinolinepiperidines, spiroisobenzofuranpiperidines, and related compds. as neuropeptide Y antagonists)

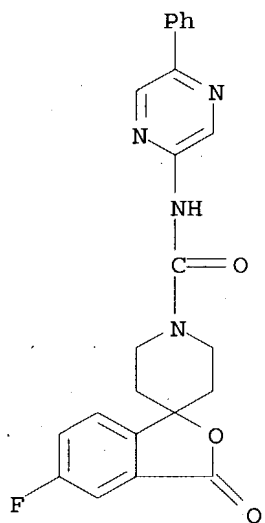
RN 328232-34-4 CAPLUS

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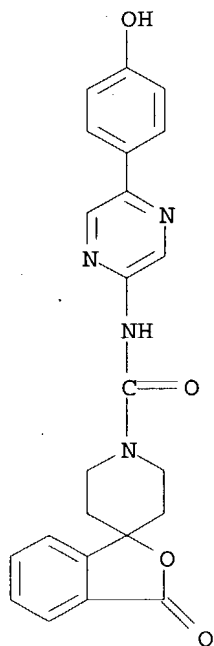
RN 328232-36-6 CAPLUS

CN Spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide,  
5-fluoro-3-oxo-N-(5-phenylpyrazinyl)- (9CI) (CA INDEX NAME)



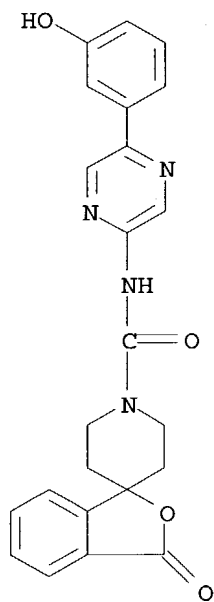
RN 328232-57-1 CAPLUS

CN Spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide,  
N-[5-(4-hydroxyphenyl)pyrazinyl]-3-oxo- (9CI) (CA INDEX NAME)



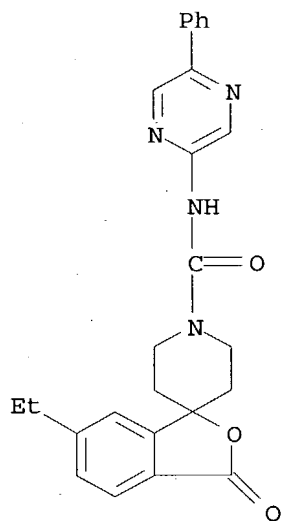
RN 328232-58-2 CAPLUS

CN Spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide,  
N-[5-(3-hydroxyphenyl)pyrazinyl]-3-oxo- (9CI) (CA INDEX NAME)

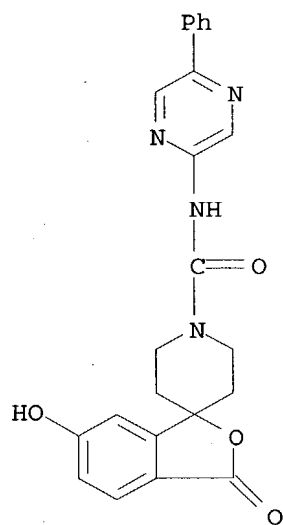


RN 328232-61-7 CAPLUS

CN Spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide,  
6-ethyl-3-oxo-N-(5-phenylpyrazinyl)- (9CI) (CA INDEX NAME)

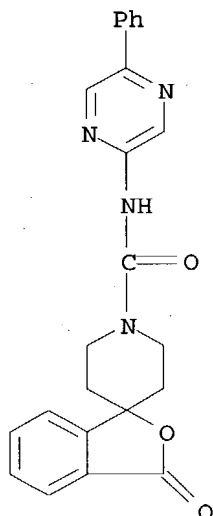


RN 328232-62-8 CAPLUS  
 CN Spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide,  
 6-hydroxy-3-oxo-N-(5-phenylpyrazinyl)- (9CI) (CA INDEX NAME)



RN 328233-00-7 CAPLUS  
 CN Spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide,  
 3-oxo-N-(5-phenylpyrazinyl)- (9CI) (CA INDEX NAME)



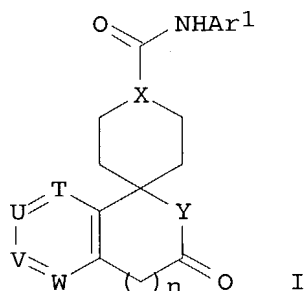


ACCESSION NUMBER: 2001:152682 CAPLUS  
 DOCUMENT NUMBER: 134:207809  
 TITLE: Preparation of spiroisindolinepiperidines, spiroisoquinolinepiperidines, spiroisobenzofuranpiperidines, and related compounds, as neuropeptide Y antagonists.  
 INVENTOR(S): Fukami, Takehiro; Kanatani, Akio; Ishihara, Akane; Ishii, Yasuyuki; Takahashi, Toshiyuki; Haga, Yuji; Sakamoto, Toshihiro; Itoh, Takahiro  
 PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 164 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 INT. PATENT CLASSIF.:  
     MAIN: C07D471-10  
     SECONDARY: A61K031-438; A61P009-00; A61P025-00; C07D491-10; C07D519-00; C07D307-94; C07D405-12; C07D471-10; C07D221-00; C07D209-00; C07D471-10; C07D221-00; C07D221-00; C07D491-10; C07D307-00; C07D221-00  
 CLASSIFICATION: 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))  
 Section cross-reference(s): 1, 63  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014376	A1	20010301	WO 2000-JP5427	20000811
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EP 1204663	A1	20020515	EP 2000-951971	20000811
EP 1204663	B1	20031029		
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EE 200200082	A	20030616	EE 2002-82	20000811

NZ 517057	A	20030829	NZ 2000-517057	20000811
JP 2002030086	A2	20020129	JP 2000-247145	20000817
JP 3411262	B2	20030526		
JP 2003104884	A2	20030409	JP 2002-271261	20000817
BG 106390	A	20021229	BG 2002-106390	20020206
NO 2002000814	A	20020415	NO 2002-814	20020219
US 2003055251	A1	20030320	US 2002-226225	20020823
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US 2003220499	A1	20031127	US 2003-453737	20030604
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			JP 2000-137692	A 20000510
			WO 2000-JP5427	W 20000811
			JP 2000-247145	A3 20000817
			US 2000-640784	A3 20000818
			US 2001-983598	A3 20011025
			US 2002-101221	A3 20020320
			US 2002-226225	A3 20020823

OTHER SOURCE(S): MARPAT 134:207809  
 GRAPHIC IMAGE:



# ABSTRACT:

Title compds. [I; Ar1 = (substituted) aryl, heteroaryl, QAr2; Ar2 = (substituted) aryl, heteroaryl; Q = bond, CO; T, U, V, W = N, (substituted) CH; X = N, CH; Y = (substituted) imino], were prepd. Thus, N-tert-butoxycarbonyl-4-piperidone was refluxed 3 h with PhCH2NH2 in PhMe to give a residue which was stirred with o-iodobenzoyl chloride and Et3N in PhMe at 80.degree. for 2 h to give N-benzyl-N-(1-tert-butoxycarbonyl-1,2,3,6-tetrahydropyridin-4-yl)-2-iodobenzamide. The latter was heated with Pd(OAc)2, Ph3P, K2CO3, and Et4NCl in MeCN at 80.degree. for 6 h to give 2-benzyl-1'-tert-butoxycarbonyl-1',6'-dihydrospiro[1H-isoindole-1,4'(5'H)-pyridine]-3(2H)-one. This was converted to N-(4-benzoylphenyl)-3-oxospiro[isoindoline-1,4'-piperidine]-1'-carboxamide, (II), which inhibited [125I]peptide YY binding to NPY Y5 receptors with IC50 = 1.2 nM. II drug formulations are given.

SUPPL. TERM: spiroisoindolinepiperidine spiroisoquinolinepiperidine  
 spiroisobenzofuranpiperidine prepn neuropeptide Y receptor  
 antagonist; antidiabetic spiroisoindolinepiperidine  
 spiroisoquinolinepiperidine spiroisobenzofuranpiperidine  
 prepn; antiobesity agent spiroisoindolinepiperidine  
 spiroisoquinolinepiperidine spiroisobenzofuranpiperidine  
 prepn; bulimia treatment spiroisoindolinepiperidine  
 spiroisoquinolinepiperidine spiroisobenzofuranpiperidine  
 prepn

INDEX TERM: Neuropeptide Y receptors  
 ROLE: BPR (Biological process); BSU (Biological study,  
 unclassified); MSC (Miscellaneous); BIOL (Biological study);  
 PROC (Process)  
 (antagonists; prepn. of spiroisoindolinepiperidines,

spiroisoquinolinepiperidines,  
spiroisobenzofuranpiperidines, and related compds. as  
neuropeptide Y antagonists)

INDEX TERM: Appetite  
(bulimia, treatment; prepn. of  
spiroisoindolinepiperidines,  
spiroisoquinolinepiperidines,  
spiroisobenzofuranpiperidines, and related compds. as  
neuropeptide Y antagonists)

INDEX TERM: Antidiabetic agents  
Antiobesity agents  
(prepn. of spiroisoindolinepiperidines,  
spiroisoquinolinepiperidines,  
spiroisobenzofuranpiperidines, and related compds. as  
neuropeptide Y antagonists)

INDEX TERM: Spiro compounds  
ROLE: BAC (Biological activity or effector, except adverse);  
BSU (Biological study, unclassified); SPN (Synthetic  
preparation); THU (Therapeutic use); BIOL (Biological  
study); PREP (Preparation); USES (Uses)  
(prepn. of spiroisoindolinepiperidines,  
spiroisoquinolinepiperidines,  
spiroisobenzofuranpiperidines, and related compds. as  
neuropeptide Y antagonists)

INDEX TERM: 328231-96-5P 328231-97-6P 328231-98-7P 328231-99-8P  
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328232-99-1P **328233-00-7P**  
ROLE: BAC (Biological activity or effector, except adverse);  
BSU (Biological study, unclassified); SPN (Synthetic  
preparation); THU (Therapeutic use); BIOL (Biological  
study); PREP (Preparation); USES (Uses)  
(prepn. of spiroisoindolinepiperidines,  
spiroisoquinolinepiperidines,  
spiroisobenzofuranpiperidines, and related compds. as  
neuropeptide Y antagonists)

INDEX TERM: 55-22-1, Isonicotinic acid, reactions 59-67-6, Nicotinic  
acid, reactions 88-65-3, 2-Bromobenzoic acid 100-07-2,  
4-Methoxybenzoyl chloride 102-52-3 107-91-5,  
Cyanoacetamide 124-68-5, 2-Amino-2-methyl-1-propanol  
609-67-6, o-Iodobenzoyl chloride 619-64-7, 4-Ethylbenzoic

acid 1137-41-3, 4-Aminobenzophenone 1779-49-3,  
Methyltriphenylphosphonium bromide 1885-14-9, Phenyl  
chlorocarbonate 3612-20-2, 1-Benzyl-4-piperidone  
4746-97-8, 1,4-Cyclohexanedione monoethylene ketal  
6144-78-1 7752-82-1, 2-Amino-5-bromopyrimidine  
10365-98-7, 3-Methoxyphenylboronic acid 13535-13-2,  
2-Amino-5-phenylpyrazine 37663-46-0 59489-71-3;  
2-Amino-5-bromopyrazine 71597-85-8, 4-Hydroxyphenylboronic  
acid 79099-07-3, N-tert-Butoxycarbonyl-4-piperidone  
87199-15-3, 3-Hydroxymethylphenylboronic acid 172733-79-8  
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ROLE: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. of spiroisindolinepiperidines,  
spiroisoquinolinepiperidines,  
spiroisobenzofuranpiperidines, and related compds. as  
neuropeptide Y antagonists)

INDEX TERM:

20577-26-8P, 2-Bromo-3-cyanopyridine 20577-27-9P,  
3-Cyano-2-hydroxypyridine 53416-46-9P 79568-32-4P  
204770-67-2P 268538-11-0P 268538-54-1P 328233-01-8P  
328233-02-9P 328233-03-0P 328233-04-1P 328233-05-2P  
328233-06-3P 328233-07-4P 328233-08-5P 328233-09-6P  
328233-10-9P 328233-11-0P 328233-12-1P 328233-13-2P  
328233-14-3P 328233-15-4P 328233-16-5P 328233-17-6P  
328233-18-7P 328233-19-8P 328233-20-1P 328233-21-2P  
328233-22-3P 328233-23-4P 328233-24-5P 328233-25-6P  
328233-26-7P 328233-27-8P 328233-28-9P 328233-29-0P  
328233-30-3P 328233-31-4P 328233-32-5P 328233-33-6P  
328233-34-7P 328233-35-8P 328233-36-9P 328233-37-0P  
328233-42-7P 328233-43-8P

ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP  
(Preparation); RACT (Reactant or reagent)  
(prepn. of spiroisindolinepiperidines,  
spiroisoquinolinepiperidines,  
spiroisobenzofuranpiperidines, and related compds. as  
neuropeptide Y antagonists)

REFERENCE COUNT:

3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD.

REFERENCE(S):

- (1) Banyu Pharma Co Ltd; WO 0027845 A 2000 CAPLUS
- (2) Hoffmann La Roche; WO 9929696 A 1999 CAPLUS
- (3) Merck & Co Inc; EP 0615977 A 1994 CAPLUS

=> log y

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
19.11	167.47

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-1.95	-1.95

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STN INTERNATIONAL LOGOFF AT 14:17:08 ON 29 NOV 2003